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REMARKS

Claims 1, 4, 6-8, 10-14 and 19 are pending in the application. All claims stand rejected.

Examiner Interview

Applicants and Applicants' attorney appreciated the opportunity to discuss the claimed invention with Examiner Francisco C. Prats during a telephonic interview held April 19, 2005. Independent claim 1 was discussed in view of the applied references (JP 9-117279 and JP 1-304882). There was not any discussion regarding proposed amendments. The thrust of Applicants' argument was that the prior art only teaches the use of sugars such as sucrose, for stabilizing unmodified SOD against dimerization/polymerization, which does not have an effect on activity, but may cause allergenic side effects; whereas the known problem associated with PC-SOD stability relates to loss of activity, and therefore would not be expected to involve a dimerization/polymerization problem. Thus, Applicants argued that the claimed invention involves the use of sucrose for solving a problem that is different problem from the known dimerization/polymerization problem associated with unmodified SOD. No agreement was reached. However, the Examiner indicated that Applicants' arguments would be given careful consideration in a written response.

Prior Art Rejection

The only outstanding issue in this case is whether claims 1, 4, 6-8, 10-14 and 19 are patentable under 35 U.S.C. §103(a) over the teachings of JP 9-117279 in view of JP 1-304882.

Those lacking ordinary skill in the art might suspect that it is possible to utilize sucrose as a stabilizing agent to prevent dimerization of PC-SOD, based on the disclosure in JP 1-304882 that sugars, such as sucrose, can be useful for stabilizing SOD against dimerization to prevent undesirable allergenic reactions. However, those having ordinary skill in the art would recognize the differences between PC-SOD and SOD, and would not expect sucrose or other sugars to have a similar stabilizing effect on PC-SOD.

The primary reference (JP 9-117279) does not recognize any stability problems with PC-SOD, and therefore does not provide any teaching relevant to the source of any stability problem with PC-SOD, or the solution to any stability problem with PC-SOD. The JP 9-

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117279 reference is relied upon solely to show that PC-SOD was known prior to Applicants' invention.

The secondary reference (JP 1-304882) does not provide any teaching relevant to PC-SOD. The JP '279 patent does not even recognize the existence of PC-SOD, and therefore does not recognize any stability problems, the source of any such stability problems, or the solution to any stability problems relating to PC-SOD. Instead, the JP '882 document only discloses that sugars, such as sucrose, may be used for stabilizing unmodified SOD against "by-products consisting mostly of dimers" (see page 3, first full paragraph of the English language translation of the JP '882 document). This is consistent with the disclosure in U.S. Patent No. 4,966,774 which states that unmodified SOD, when stored in a powder form "suffer[s] from clouding caused by polymerization" (column 1, lines 27-32). The polymerization referred to in the '774 patent apparently encompasses dimerization, whereas the "by-products consisting mostly of dimers" disclosed in the JP '882 document apparently refers to small amounts of trimers and other oligomeric products in addition to the dimers. Sugars, including sucrose, are disclosed as stabilizing agents that prevent polymerization reactions, including dimerization, of unmodified SOD.

Notably, it is disclosed in the JP '882 document that the by-products (dimers and other polymerization products) do not suffer any decrease in enzymatic activity. Instead, the problem is that the dimers and other polymerization products "may have allergenic side effects" and, therefore, "the generation of such substances must be prevented" (see page 3, second full paragraph of the English language translation of the JP '882 document).

As disclosed in the U.S. Patent No. 5,109,118, PC-SOD is derived by bonding a lecithin derivative to an amino group or a carboxyl group of the SOD. Those having ordinary skill in the art would appreciate that by utilizing these functional groups of the SOD for attachment of the lecithin derivatives, dimerization and other polymerization reactions utilizing these functional groups of the SOD are prevented. Accordingly, those having ordinary skill in the art would appreciate that dimerization and other polymerization by-products that form during storage of unmodified SOD will not occur during storage of PC-SOD. This conclusion is consistent with the prior art, which does not disclose dimerization or other polymerization problems with PC-SOD.

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Those having ordinary skill in the art would understand the mechanisms by which dimerization/polymerization occur with SOD, the mechanisms by which lecithin derivatives are bonded to SOD, and that the dimerization/polymerization problems associated with SOD would not occur with PC-SOD. In fact, the prior art of record has completely failed to recognize any stability problem with PC-SOD. The Applicants have discovered that while there is not any dimerization/polymerization problem with PC-SOD, there is an entirely different, unrelated problem associated with degradation of the lecithin moieties of the PC-SOD. As admitted at page 2, lines 5-8, there was a recognized problem with the reduction of activity of PC-SOD due to long-term storage. Those having ordinary skill in the art would have understood that this is a different problem than the dimerization/polymerization problem of SOD for the reasons stated above, and because the dimerization/polymerization problem known in the prior art for SOD is not associated with a loss of activity, but instead produces by-products that may have an allergenic side effect.

While the loss of activity associated with long-term storage of PC-SOD was known, the source of the problem and its solution were unknown. Applicants discovered that the problem is caused by degradation of the lecithin moiety. Not only were Applicants the first to discover the source of the problem, but, in addition, Applicants were first to discover an unobvious solution to the problem. There is nothing in the prior art suggesting that sugars, such as sucrose, may be used for stabilizing lecithin-modified proteins against lecithin moiety degradation. Certainly, the teaching in the prior art that sugars, such as sucrose, may be used for preventing dimerization of unmodified proteins would not have suggested the claimed invention.

The fact that the prior art used similar stabilizing agents to solve an unrelated problem (dimerization/polymerization of unmodified SOD) does not lead those having ordinary skill in the art toward a discovery of the source of a stability problem leading to loss of activity of PC-SOD during long-term storage, and does not lead one having ordinary skill in the art to the particular solution claimed. The use of sucrose for solving an entirely different and unrelated

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problem was unexpected and, therefore, was not obvious. Accordingly, reversal of the rejection is appropriate.

CONCLUSION

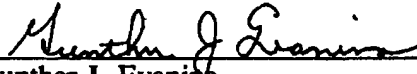
In view of the above remarks, it is respectfully submitted that the application is in condition for allowance and notice of the same is earnestly solicited.

Respectfully submitted,

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Date


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